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The School of Medicine

DEPARTMENT OF MICROBIOLOGY

November 16, 1952

Dr. J. Lederberg
Department of Genetics
College of Agriculture
University of Wisconsin
Madison 6, Wisconsin

Dear Dr. Lederberg,

Thank you for your letter of November 13th informing me of the existence of lambda-2. At the time of initial assay of our purified K12-lambda stock, I had plated an excess of virus but must have overlooked the appearance of clear lytic plaques. We can now, I believe, get enough information from lambda - W1485 for comparison with lambda-2 - K12 (or W1485) to check our cytological and physiological observations on these lytic systems.

I have heard that there are mutants of K12 resistant to the action of lambda but which do not carry it. Perhaps, by replica plating these cells on lambda-spread plates after the action of a mutagen, one might obtain lambda-sensitive cells (unable to grow in presence of lambda). This test would differentiate sensitive cells from those clones able to become lysogenic or those resistant cells not carrying lambda (both would grow on lambda plate).

However, because of ~~these~~ lytic mutants, one should probably use caution in applying only a minimal effective concentration of lambda on the replica plate. In the case of isolation of B/1 mutants by replica plating, it has been my experience that B/1, tryp are more difficult to isolate than other B/1's (presumably B/1,5). This, I think, is due to the presence of an unfortunately large initial concentration of T1h mutants in my stock; these attack B/1, tryp rather than B/1,5. This could also account for the change in preponderance of the two types of bacterial mutants in Bryson's comparison of spontaneous and induced B/1 mutants were different numbers of susceptible cells used in the two conditions, thus allowing a greater chance for T1h production (or host transformation).

We have been unable to isolate a single B/S^r (120 and 240 gamma SM/cc of nutrient agar) by replica plating, even from confluent growth plates. If we are not transferring enough cells on our velveteen, we may be able to overcome this by plating out the "jackpot" tubes from fluctuation tests and replica plate from those plates.

We have not studied thoroughly as yet the chromosomal cytology of W1485 exposed to lambda under lysophoretic conditions but will do so shortly. Dr. R.G.E. Murray, one of the few level-headed bacterial cytologists, in my estimation, has found a temporary dirsuption of

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Sincerely yours,

Philip E. Hartman

normal nuclear events in cells becoming lysogenic to Sal. typhimurium (Boyd) phages, via application of external phage. This might indicate an actual nuclear site of the provirus. However, if the provirus locus is the site of the factor itself, it would be more difficult to explain the disappearance of provirus in a substantial proportion of the population as the result of rapid growth in certain media (Clarke). Of course, if it is true that the "transduced" genetic markers found by the Plough group can revert en masse spontaneously, more intricate explanations are appropriate for other microbial systems. Perhaps rapid transfer is a requisite in the loss of the transduced system, also.

The other day I ran into a letter you wrote several years ago to the editors of SCIENCE, putting forth briefly a theory on the possible mechanism of tumor origin. It seems to me to be an overall theory of great value and one which, when brought up to date to include the recently gained knowledge of latent and masked viruses, is well worth calling attention to again in more full form. The recent studies, especially in Britian, of the regulation of growth (cell division) by a limited energy supply (glucose) in some tissues throws additional light on the problem. In my own personal estimation, the working hypotheses of the cancer people are largely too narrow, each in its own direction, to be effective in a long range study. A multifold proposal such as yours would encourage a broader outlook among this group. Even if time has taken its toll on the simplicity of your earlier statement, the general theses could well be recalled.

Dr. George Gomori has purified triphenyltetrazolium chloride (dissolving in small volume absolute alcohol and pouring the solution into 4-5 volumes of ether) from a contaminant he believes might be lead tetraacetate. You mught find a more purified reagent more useful in your studies of "labled" fusion cells. I intend attempting purification of blue tetrazolium by similar methods (based on the information in the papers of Selifman and Rutenburg) but have not as yet found time to do so.

A note on copper-induced "transformation" of E. coli has now appeared (Weed, L.L. & Longfellow, D. 1952 PROC 3rd INT. CONGR. BIOCH., Paris, p. 96).

Dr. Gots and I have dropped our pursuit of lysogenicity in E. coli B for the present time. It is difficult to explain all of the positive results, few as they are, on the basis of contamination alone (e.g. with E. coli W), but we have not been able to get positive results with anything even resembling consistency and are dropping the project temporarily in favor of other projects now in progress. Dr. Tom Nelson will probably be sorry to hear of this failure, but perhaps it is good to have one bacterial strain which is neither lysogenic nor colicine-producing!